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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,184	11/16/2001	Yin Hwee Tan	117-363	9483

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EXAMINER	
KHARE, DEVESH	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/914,184	TAN ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30 and 38-41* is/are pending in the application.

4a) Of the above claim(s) *30 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-29,38,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's amendments and remarks filed on 08/16/2004 are acknowledged.

Claims 1-21 and 31-37 have been cancelled. Claims 22 and 28 have been amended.

New claims 40 and 41 have been added. Claims 30 and 39 have been withdrawn.

The rejection of claims 22-29 and 38, under 35 U.S.C., 112, second paragraph, has been overcome through applicants' amendments. The objection of claims 22 and 29 has been overcome through applicant's amendments and remarks.

During the course of reconsideration of the application, a prior art reference not previously applied in the 35 U.S.C. 103(a) rejection is applied here (see rejection below).

Claims 22-29,38,40 and 41 are currently pending in this application.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 22-29,38 and newly added claims 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Najarian (WO 98/19670) in combinations with Luscri (Abs. of the Annual meeting of the American Society, vol.83, 1983, page A130) in view of Sjogren (U.S. Patent 5,380,879).

Claims 22-29,38,40 and 41 are drawn to a method of treating a host having a flavivirus or rhabdovirus infection, by administering to the host an effective amounts of an interferon and atleast one compound selected from the group consisting of 5-membered cyclic nucleoside having the formula (I) and pharmaceutically acceptable metabolites,

2,4-diaminopyrimidines (formula V) and a quinazoline derivative (formula VI). Dependent claim limitations claimed include the flavivirus selected from yellow fever virus, kunjin virus, dengue virus, hepatitis C virus, and encephalitis virus; rhabdovirus selected from vesicular stomatitis virus (VSV) and rabies virus; interferon is a human interferon or selected from interferon α2, interferon α8 (specific activity 0.6-1.5 x 10^9 IU per mg protein) and interferon β (specific activity 4-8 x 10^8 IU per mg protein); and administration to the host in respective amounts. Dependent claim 29 includes the compounds selected from the group consisting of cyclopentenyl cytosine, mycophenolic acid, amanatadine hydrochloride, -azauridine and antibiotics. Depenedent newly added claim 40 include the bases selected from the group consisting of formulas i-viii. Newly added claim 41 include a method of treating the host having a flavivirus or rhabdovirus infection by administering the host an interferon and at least one aminoadamantane of formula IV producing a synergistic effect.

Najarian teaches a method for treatment of hepatitis C infection with a composition comprising a nucleoside analog, a quinoline antibiotic and an amantadine anti-viral agent including the interferon α (see abstract). The preferred interferon is α, however interferon β can also be used (page 6, line 1). The said composition can be administered separately or together (page 7, last para.). Najarian discloses the interferon doses in the range of 5-2.5 million units (page 14, Example 1). The nucleoside analogs such as ribavirin, lamivudine, vidarabine and genciclovir; amantadine derivatives; and quinolone antibiotics such as ofloxacin, levofloxacin,

ciprofloxacin and norfloxacin are disclosed (page 6, 2nd – 4th para.). The teachings of Najarian does render the use of a composition comprising an interferon and a nucleoside analog, a quinoline antibiotic or an amantadine anti-viral agent to treat flavivirus or rhabdovirus infection prima facie obvious. Najarian differs from the instantly claimed invention that Najarian does not explicitly teaches the use of mycophenolic acid compounds in the composition.

Luscri teaches the synergistic effects of human interferons in combination with amantadine or rimantadine in treating the infections caused by viruses of yellow fever, west nile or Japanese encephalitis (abstract).

Sjogren teaches the pharmaceutical compositions containing mycophenolic acid compounds useful as anti-viral agents (col. 17, lines 20-30) specifically the hepatitis (col.17, line 42). The mycophenolic acid compounds are represented by the formula I (col.2, line 25).

Therefore, one of ordinary skill in the art would have found the applicants claimed method of treating a host having a flavivirus or rhabdovirus infection selected from yellow fever virus, kunjin virus, dengue virus, hepatitis C virus, and encephalitis virus, by administering to the host the combination of an interferon and atleast one compound selected from the group consisting of 5-membered cyclic nucleoside having the formula (I) and pharmaceutically acceptable metabolites, 2,4-diaminopyrimidines (formula V) and a quinazoline derivative (formula VI) or administering the host the combination of

an interferon and at least one aminoadamantane of formula IV producing a synergistic effect, to have been obvious at the time the invention was made having the above cited references before him. Since Najarian teaches a method for treatment of hepatitis C infection with a composition comprising interferon, nucleoside analogs and quinolone antibiotics; Luscri teaches the synergistic effects of human interferons in combination with amantadine or rimantadine in treating the infections caused by viruses of yellow fever, west nile or Japanese encephalitis; and Sjogren teaches the pharmaceutical compositions containing mycophenolic acid compounds useful as anti-viral agents specifically the hepatitis, one skilled in the art would have a reasonable expectation for success in combining the teachings of these references to accomplish a method of treating a host having a flavivirus or rhabdovirus infection. One would be motivated to use interferon with other anti-viral agents in order to reduce the cost of interferon therapy (Najarian: page 5, 4th para.) or to take advantage of diverse modes of antiviral activity, and to lower the use of potential antiviral-nucleosides which might be toxic.

Response to Arguments

Applicant's arguments traversing the rejection of claims 22-29 and 38 under 35 U.S.C 103(a) have been fully considered but they are not persuasive. These arguments also fail to obviate the rejection of newly added claims 40 and 41.

Applicant argues, "there is no reference in Sjogren to the possible use of mycophenolic acid derivatives in the treatment of such viral infections" and "there is no

teaching or suggestion in either of the cited references that a combination of interferon and an aminoadamantane compound would have a synergistic effect".

It is noted that Sjogren reference is silent of disclosing the use of mycophenolic acid derivatives in the treatment of infection due to hepatitis C virus however Sjogren teaches the pharmaceutical compositions containing mycophenolic acid compounds useful as anti-viral agents (col. 17, lines 20-30) specifically the hepatitis (col.17, line 42).

The newly cited Luscri refernce teaches the synergistic effects of human interferons in combination with amantadine or rimantadine in treating the infections caused by viruses of yellow fever, west nile or Japanese encephalitis (abstract).

Also, Najarian teaches a method for treatment of hepatitis C infection with a composition comprising interferon, nucleoside analogs and quinolone antibiotics.

The invention as a whole is that of a method of treating a host having a flavivirus or rhabdovirus infection selected from yellow fever virus, kunjin virus, dengue virus, hepatitis C virus, and encephalitis virus, by administering to the host the combination of an interferon and atleast one compound selected from the group consisting of 5-membered cyclic nucleoside having the formula (I) and pharmaceutically acceptable metabolites, 2,4-diaminopyrimidines (formula V) and a quinazoline derivative (formula VI) or administering the host the combination of an interferon and at least one aminoadamantane of formula IV producing a synergistic effect. The combination of these ingredients do not appear to provide benefits which would be unexpected by one ordinary skill in the art. It has been previously been held that it is obvious to combine

ingredients which have been separately employed for a particular purpose in order to obtain the expected combination of benefits (In re Greenfield, 571 F2d 1185, 197 USPQ 227 (CCPA 1978)) and that no patentable invention resides in combining old ingredients of known characteristics where the results obtained thereby are no more than the additive effect of the ingredient (In re Sussman, 1943 C.D. 518; In re Huellmantel, 139 USPQ 496; In re Crockett et al., 1266 USPQ 186).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is 571-272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD.
Art Unit 1623
November 8,2004

JAMES O. WILSON
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